Office Action Summary	Application No.	Applicant(s)	
	10/595,230	LINDSTROM ET AL.	
	Examiner	Art Unit	
	Rita J. Desai	1625	

-- *The MAILING DATE of this communication appears on the cover sheet with the correspondence address* --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 June 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *4-10,12,13,23-27,46-49,55-57,62-66,77-79,81-87 and 89-111* is/are pending in the application.

4a) Of the above claim(s) *87,89,90,104,110 and 111* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *4-10,12,13,23-27,46-49,55-57,62-66,77-79,81-86 and 91-103* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

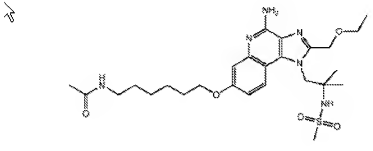
1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *3/28/06,5/29/09*.
4) ☒ Interview Summary (PTO-413) Paper No(s)/Mail Date *7/21/09*.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicants had originally elected Group II.

Group II, claim(s) 4-10, 12, 13, 23-27, 46-49, 55-57, 62-66, 77-79, 81-86, 91-103, drawn to compounds and compositions of formula I wherein R1 and R2 are other than those given in group I above. A further election of a single disclosed species is required.

And elected the species



The examiner has further restricted group II into

Group IIa :- Claims 4-10, 12, 13, 23-27, 46-49, 55-57, 62-66, 77-79, 81-86, 91-103, drawn to compounds and compositions of formula I wherein R1 and R3 are alkyl chains with a N and R2 is an alkyl or an alkoxy group.

Group IIb :- Claims 4-10, 12, 13, 23-27, 46-49, 55-57, 62-66, 77-79, 81-86, 91-103, drawn to compounds and compositions of formula I wherein only R1 is a alkyl chains with a N and R2 is an alkyl or an alkoxy group.

In a telephonic election Mr. Hunter Baker elected group IIa with traverse for prosecution..

Claim Rejections - 35 USC § 103

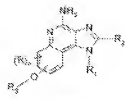
The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 4-10, 12, 13, 23-27, 46-49, 55-57, 62-66, 77-79, 81-86, 91-103 are rejected under 35 U.S.C. 103(a) as being obvious over WO 2005202999.

.The applied reference has a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art only under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 103(a) might be overcome by: (1) a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not an invention "by another"; (2) a showing of a date of invention for the claimed subject matter of the application which corresponds to subject matter disclosed but not claimed in the reference, prior to the effective U.S. filing date of the reference under 37 CFR 1.131; or (3) an oath or declaration under 37 CFR 1.130 stating that the application and reference are currently owned by the same party and that the inventor named in the application is the prior inventor under 35 U.S.C. 104, together with a terminal disclaimer in accordance with 37 CFR 1.321(c). This rejection might also be overcome by showing that the reference is disqualified under 35 U.S.C. 103(c) as prior art in a rejection under 35 U.S.C. 103(a). See MPEP § 706.02(l)(1) and § 706.02(l)(2).

Applicants claims are drawn to the compounds of the formula



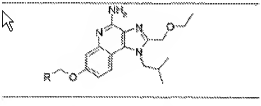
II

wherein R1 and R3 are both alkyl with a N group.

Scope & Content of Prior Art MPEP 2141.01

The reference teaches similar compounds . See foe example pages 188, 203 eg 120.

The compounds have the same substituent for the R1 position. The substituent at the R3 position can also be the same as applicants R3.



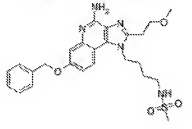
Compound 29 has R with an N containing het ring.

29	1-(3-Bromopropyl)pyrrole	
30	2-Chlorobenzyl chloride	

See eg 50 which teaches the R1 substituent same as applicants.

Example 50

N-{4-[4-Amino-7-benzyloxy-2-(2-methoxyethyl)-1H-imidazo[4,5-c]quinolin-1-yl]butyl}methanesulfonamide



Also see examples 51,52.

Difference between Prior Art and the claims MPEP 2141.02

The difference is that these substituents are not show on a single compound together.

But the teaching that these substituents can be substituted is there. The use of the compounds is also the same.

Prima Facie Obviousness , Rational and Motivation MPEP 2142-2413

As the prior art teaches all the variables, one of skill in the art would be motivated to modify the compounds to obtain the compounds of the invention.

See KSR, 82 USPQ2d at 1396. 2007.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned

with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 4-10, 12, 13, 23-27, 46-49, 55-57, 62-66, 77-79, 81-86, 91-103 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-43 of copending Application No. 10/595103. Although the conflicting claims are not identical, they are not patentably distinct from each other because similar substituents are shown for R2 and R3 and R1positions. All the variables are disclosed and it would be obvious for one skilled in the art to interchange the substitutents to obtain the compounds of the invention. See the rejection above.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 4-10, 12, 13, 23-27, 46-49, 55-57, 62-66, 77-79, 81-86, 91-103 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a few substituents with alkyl N groups for R2 and R3, does not reasonably provide enablement for all the various substitutents generically disclosed. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue". These factors include 1) the breadth of the claims, 2) the nature of the invention, 3) the state of the prior art, 4) the level of one of ordinary skill, 5) the level of predictability in the art, 6) the amount of direction provided by the inventor, 7) the existence of working examples, and 8) the quantity of experimentation needed to make or use the invention based on the content of the disclosure. In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

1) The breadth of the claims: The instant claims encompass many compounds from an aromatic carbocyclic moiety to an aromatic carbocyclic moiety having many large electron withdrawing and bulky groups substituted on it to a moiety having many heterocyclic rings. These compounds cover a very wide range of compounds.

wherein,

R_3 is selected from the group consisting of

-Z-Y-R_6,

-Z-Y-X-Y-R_6,

-Z-R_5,

-Z-Het,

-Z-Het'-R_6, and

-Z-Het'-Y-R_6;

Z is selected from the group consisting of alkylene, alkenylene, and alkynylene, wherein alkylene, alkenylene, and alkynylene can be optionally interrupted with one or more -O- groups;

R_5 is selected from the group consisting of alkyl, alkoxy, hydroxy, halogen, and trifluoromethyl;

n is 0 or 1;

R_6 is selected from the group consisting of

-R_5,

-X-R_6,

-X-Y-R_6,

-X-Y-X-Y-R_4, and

-X-R_5;

R_2 is selected from the group consisting of

-R_4,

-X-R_4,

-X-Y-R_4, and

-X-R_5;

X is selected from the group consisting of alkylene, alkenylene, alkynylene, arylene, heteroarylene, and heterocyclylene wherein the alkylene, alkenylene, and alkynylene groups can be optionally interrupted or terminated with arylene, heteroarylene, or heterocyclylene; and optionally interrupted by one or more -O- groups;

Y is selected from the group consisting of

-$S(O)_{0-2}$-,

-$S(O)_2$-$N(R_8)$-,

-$C(R_8)$-,

-$C(R_8)$-O-,

-O-$C(R_8)$-,

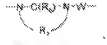
-O-C(O)-O-,

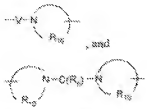
-$N(R_8)$-O-,

-$C(R_8)$-$N(R_8)$-,

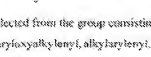
-O-$C(R_8)$-$N(R_8)$-,

-$C(R_8)$-$N(OR_8)$-,





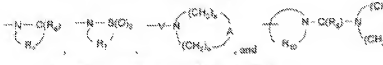
, and



;

R_4 is selected from the group consisting of hydrogen, alkyl, alkenyl, alkynyl, aryl, arylalkylenyl, aryloxyalkylenyl, alkylarylenyl, heteroaryl, heteroarylalkylenyl, heteroaryloxyalkylenyl, alkylheteroarylenyl, and heterocyclyl wherein the alkyl, alkenyl, alkynyl, aryl, arylalkylenyl, aryloxyalkylenyl, alkylarylenyl, heteroaryl, heteroarylalkylenyl, heteroaryloxyalkylenyl, alkylheteroarylenyl, and heterocyclyl groups can be unsubstituted or substituted by one or more substituents independently selected from the group consisting of alkyl, alkoxy, hydroxyalkyl, haloalkyl, haloalkoxy, halogen, nitro, hydroxy, mercapto, cyano, aryl, aryloxy, arylalkylenoxy, heteroaryl, heteroaryloxy, heteroarylalkylenoxy, heterocyclyl, amino, alkylamino, dialkylamino, (dialkylamino)alkylenoxy, and in the case of alkyl, alkenyl, alkynyl, and heterocyclyl, oxo;

R_5 is selected from the group consisting of



;

R_6 is selected from the group consisting of =O and =S;

R_7 is C_{2-3} alkylene;

R_8 is selected from the group consisting of hydrogen, alkyl, alkoxyalkylenyl, and arylalkylenyl;

R_9 is selected from the group consisting of hydrogen and alkyl;

R_{10} is C_{2-8} alkylene;

A is selected from the group consisting of -O-, -C(O)-, $-S(O)_{0-2}$-, and $-N(R_4)$-;

Het is heterocyclyl which can be unsubstituted or substituted by one or more substituents independently selected from the group consisting of alkyl, alkoxy, haloalkyl, haloalkoxy, halogen, nitro, hydroxy, hydroxyalkyl, mercapto, cyano, aryloxy, arylalkylenoxy, heteroaryloxy,

and so on and so on.

2) The nature of the invention: The invention is a (highly) substituted tricyclic compound for cytokine biosynthesis., treating viral infections.

3) The state of the prior art: There are few compounds in the prior art which have similar substituents. The state of the prior art is that it involves screening in vitro and invivo to determine which compounds exhibit the desired pharmacological activities. There is no

absolute predictability and no established correlation between in vitro activity for cytokine biosynthesis as the in vitro data is not a reliable predictor of success even in view of the seemingly high level of skill in the art. The existence of these obstacles establishes that the contemporary knowledge in the art would prevent one of ordinary skill in the art from accepting any therapeutic regimen on its face..

4) The level of one of ordinary skill: The ordinary artisan is highly skilled.

5) The level of predictability in the art: It is noted that the pharmaceutical art is unpredictable , requiring each embodiment to be individually assessed for physiological activity. In re Fisher, 427 F. 2d 833, 166 USPQ 18(CCPA 1970) indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statue. The level of unpredictability is in the art is very high. The compounds which differ by a methyl group also show different properties, for e.g. theophylline and caffeine. One of them is a bronchodilator and they differ only by a methyl group.
Also it is difficult to synthesize compounds
As stated in the preface to a recent treatise:

"Most non-chemists would probably be horrified if they were to learn how many attempted syntheses fail, and how inefficient research chemists are. The ratio of successful to unsuccessful chemical experiments in a normal research laboratory is far below unity, and synthetic research chemists, in the same way as most scientists, spend most of their time working out what went wrong, and why. Despite the many pitfalls lurking in organic synthesis, most organic chemistry textbooks and research articles do give the impression that organic reactions just proceed smoothly and that the total synthesis of complex natural products, for instance, is maybe a labor-intensive but otherwise undemanding task. In fact, most syntheses of structurally complex natural products are the result of several years of hard work by a team of chemists, with almost every step requiring careful optimization. The final synthesis usually looks quite different from that originally planned, because of unexpected difficulties encountered in the initially chosen synthetic sequence. Only the seasoned practitioner who has experienced for himself the many failures and frustrations which the development (sometimes even the repetition) of a synthesis

usually implies will be able to appraise such work .....Chemists tend not to publish negative results, because these are, as opposed to positive results, never definite (and far too copious) ....." Dorwald F. A.

Side Reactions in Organic Synthesis, 2005, Wiley: VCH, Weinheim pg. IX of Preface.

6) The amount of direction provided by the inventor: The inventor provides very little direction in the instant specification. There are about 10 examples with both R2 and R3 being an alkyl –N group. There is no data provided to show that these compounds do indeed have cytokine biosynthesis activity.

7) The existence of working examples: The instant specification have very few working examples. The prior art does not teaches a limited examples and applicants claim is very broad. Applicants have not shown a reduction to practice commensurate to the scope of the claims.

8) The quantity of experimentation needed to make or use the invention based on the content of the disclosure: Since there are no working examples, the amount of experimentation is very high and burdensome.

Taking the above eight factors into consideration, it is not seen where the instant specification enables the ordinary artisan to make and/or use the instantly claimed invention.

Genetech Inc Vs Nova Nordisk 42 USPQ 2d 1001.

"A patent is not a hunting license. It is not a reward for search but compensation for its successful conclusion and patent protection is granted in return for an enabling disclosure of an invention , not for vague intimations of general ideas that may or may not be workable."

MPEP 2164.01(a) states, "A conclusion of lack of enablement means that, based on the evidence regarding each of the above factors, the specification, at the time the application was flied, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue

experimentation. In re Wright, 999 F.2d 1557,1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993)." That conclusion is clearly justified here. Thus, undue experimentation will be required to practice Applicants' invention.

Conclusion

4-10, 12, 13, 23-27, 46-49, 55-57, 62-66, 77-79, 81-86, 91-103 are rejected.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Rita J. Desai whose telephone number is 571-272-0684. The examiner can normally be reached on Monday - Friday, flex time..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Janet Andres can be reached on 571-272-0867. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Rita J. Desai/
Primary Examiner, Art Unit 1625

July 24, 2009